

REMARKS

Claims 1-14 and 29-40 are pending in this application. It is respectfully requested that this application be amended by amending claims 1, 2, 14, 29, 32, 36, 39 and 40 and adding claims 41-45.

Claim 1 has been amended to correct -N(C(O)CF₃).

Claim 2 has been amended to correct the case of SO₂(C₁-C₆ alkyl).

Claim 12 has been amended to add "4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine - (disclosed on page 11, line 2 of the specification); [3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine - (disclosed on page 10, line 32 of the specification) and [2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine - (disclosed on page 16, line 11 of the specification).

Claim 13 has been amended to delete the phrases "such as fibromyalgia" and "including cerebral ischemia" and to add "excitotoxic neuronal damage." Support for the addition of "excitotoxic neuronal damage" in claim 13 is found on page 24, line 27 of the specification.

New claim 41 depends from claim 13 and defines the pain perception as fibromyalgia.

New claim 42 depends from claim 13 and defines the ischemic neuronal damage as cerebral ischemia.

Claim 14 has been amended to delete the phrase "such as depression and postpartum depression" and delete ", including a human".

New claim 43 depends from claim 14 and defines the mood disorders as depression or postpartum depression.

New claim 44 depends from claim 14 and defines the ischemic neuronal damage as cerebral ischemia.

New claim 45 depends from claim 14 and defines a mammal as a human.

Claim 29 has been amended to replace "R24 and R25" with "R₂₄ and R₂₅".

Claim 36 has been amended to delete the word "including" in line 2 of the claim.

Claim 39 has been amended to depend from claim 44 and to delete "excitotoxic

neuronal damage” which has been added to claim 13.

Claim 40 has been amended to place a period at the end of the claim.

In view of these amendments, it is respectfully requested that the objections to claims 2, 13, 14, and 29 and the rejection of claims 1-14 and 29-40 under 35 USC 112, second paragraph be withdrawn.

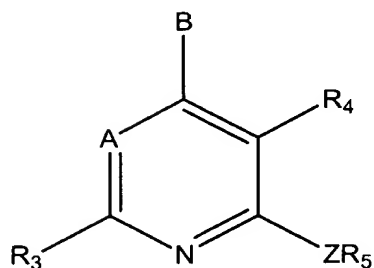
Respectfully submitted,

A handwritten signature in black ink, appearing to read "Janet I. Cord", with a long horizontal flourish extending to the right.

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Claim 1 (Twice Amended). A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is N;

B is -NR₁R₂, -CR₁R₂R₁₁, -C(=CR₂R₁₂)R₁, -NHCHR₁R₂, -OCHR₁R₂, -SCHR₁R₂, -CHR₂OR₁, -CHR₁OR₂, -CHR₂SR₁, -C(S)R₂, -C(O)R₂, -CHR₂NR₁R[2]₂, -CHR₁NHR₂, -CHR₁N(CH₃)R₂, or -NR₁₂NR₁R₂;

Z is NH, O, S, -N (C₁-C₂ alkyl)-, [-NC(O)CF₃] N(C(O)CF₃)- or -C(R₁₃R₁₄)-, wherein R₁₃ and R₁₄ are each, independently, hydrogen, trifluoromethyl or methyl, or one of R₁₃ and R₁₄ is cyano and the other is hydrogen or methyl, or -C(R₁₃R₁₄) is a cyclopropyl group, or Z is nitrogen or CH and forms a five or six membered heterocyclic ring fused with R₅, which ring optionally comprises two or three further hetero members selected independently from oxygen, nitrogen, NR₁₂, and S(O)_m, and optionally comprises from one to three double bonds, and is optionally substituted with halo, C₁-C₄ alkyl, -O(C₁-C₄ alkyl), NH₂, NHCH₃, N(CH₃)₂, CF₃, or OCF₃, with the proviso that said ring does not contain any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and does not comprise more than two oxygen or S(O)_m heterologous members;

R₁ is C(O)H, C(O)(C₁-C₆ hydrocarbyl), C(O)(C₁-C₆ hydrocarbylene)(C₃-C₈ cyclohydrocarbyl), C(O)(C₃-C₈ cyclohydrocarbylene)(C₃-C₈ cyclohydrocarbyl), C(O)(C₁-C₆ hydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), -C(O)(C₃-C₈ cyclohydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), C₁-C₆ hydrocarbyl, C₃-C₈ cyclohydrocarbyl, C₄-C₈ heterocyclohydrocarbyl, -(C₁-C₆ hydrocarbylene)(C₃-C₈ cyclohydrocarbyl), C₃-C₈ cyclohydrocarbylene)(C₃-C₈ cyclohydrocarbyl), -(C₁-C₆ hydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), -(C₃-C₈ cyclohydrocarbylene)(C₄-C₈ heterocyclohydrocarbyl), or -O-aryl, or -O-(C₁-C₆ hydrocarbylene)-aryl; wherein said aryl, C₄-C₈ heterocyclohydrocarbyl, C₁-C₆ hydrocarbyl, C₃-C₈ cyclohydrocarbyl, C₃-C₈ cyclohydrocarbylene, and C₁-C₆ hydrocarbylene groups may each independently be optionally substituted with from one to six

fluoro and may each independently be optionally substituted with one or two substituents R_8 independently selected from the group consisting of C_1 - C_4 hydrocarbyl, $-C_3$ - C_8 cyclohydrocarbyl, hydroxy, chloro, bromo, iodo, CF_3 , $-O$ -(C_1 - C_6 hydrocarbyl), $-O$ -(C_3 - C_5 cyclohydrocarbyl), $-O$ -CO-(C_1 - C_4 hydrocarbyl), $-O$ -CO-NH(C_1 - C_4 hydrocarbyl), $-O$ -CO-N(R_{24})(R_{25}), $-N$ (R_{24})(R_{25}), $-S$ (C_1 - C_4 hydrocarbyl), $-S$ (C_3 - C_5 cyclohydrocarbyl) $-N$ (C_1 - C_4 hydrocarbyl)CO(C_1 - C_4 hydrocarbyl), $-NH$ CO(C_1 - C_4 hydrocarbyl), $-COO$ (C_1 - C_4 hydrocarbyl), $-CONH$ (C_1 - C_4 hydrocarbyl), $-CONC_1$ - C_4 hydrocarbyl)(C_1 - C_2 hydrocarbyl), CN , NO_2 , $-OSO_2$ (C_1 - C_4 hydrocarbyl), S^+ (C_1 - C_6 hydrocarbyl)(C_1 - C_2 hydrocarbyl), $-SO$ (C_1 - C_4 hydrocarbyl) and $-SO_2$ (C_1 - C_4 hydrocarbyl); and wherein the C_1 - C_6 hydrocarbyl, C_1 - C_6 hydrocarbylene, C_3 - C_8 cyclohydrocarbyl, C_3 - C_8 cyclohydrocarbylene, and C_3 - C_8 heterocyclohydrocarbyl moieties of R_1 may optionally independently contain from one to three double or triple bonds; and wherein the C_1 - C_4 hydrocarbyl moieties and C_1 - C_6 hydrocarbyl moieties of R_8 can optionally independently be substituted with hydroxy, amino, C_1 - C_4 alkyl, aryl, $-CH_2$ -aryl, C_3 - C_5 cycloalkyl, or $-O$ -(C_1 - C_4 alkyl), and can optionally independently be substituted with from one to six fluoro, and can optionally contain one or two double or triple bonds; and wherein each heterocyclohydrocarbyl group of R_1 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12} ;

R_2 is hydrogen, C_1 - C_{12} hydrocarbyl, C_3 - C_8 cyclohydrocarbyl, C_4 - C_8 heterocyclohydrocarbyl, $-(C_1$ - C_6 hydrocarbylene)(C_3 - C_8 cyclohydrocarbyl), $-(C_3$ - C_8 cyclohydrocarbylene)(C_3 - C_8 cyclohydrocarbyl), $-(C_1$ - C_6 hydrocarbylene)(C_4 - C_8 heterocyclohydrocarbyl), $-(C_3$ - C_6 cyclohydrocarbylene)(C_4 - C_8 heterocyclohydrocarbyl), aryl, $-(C_1$ - C_6 hydrocarbylene)aryl, or $-(C_3$ - C_8 cyclohydrocarbylene)(aryl); wherein each of the foregoing R_2 groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro, and C_1 - C_6 alkyl, wherein one of said one to three substituents can further be selected from bromo, iodo, C_1 - C_6 alkoxy, $-OH$, $-O$ -CO-(C_1 - C_6 alkyl), $-O$ -CO-N(C_1 - C_4 alkyl)(C_1 - C_2 alkyl), $-S$ (C_1 - C_6 alkyl), $-S(O)$ (C_1 - C_6 alkyl), $-S(O)_2$ (C_1 - C_6 alkyl), S^+ (C_1 - C_6 alkyl)(C_1 - C_2 alkyl)I', CN , and NO_2 ; and wherein the C_1 - C_{12} hydrocarbyl, $-(C_1$ - C_6 hydrocarbylene), and cyclohydrocarbyl groups of 5 - 8 carbon atoms, cyclohydrocarbylene groups of 5 to 8 carbon atoms and heterocyclohydrocarbyl groups of 5 to 8 atoms of R_2 may optionally independently contain from one to three double or triple bonds; and wherein each heterocyclohydrocarbyl group of R_2 contains from one to three heteromoieties selected from oxygen, $S(O)_m$, nitrogen, and NR_{12} ;

or when R_1 and R_2 are as in $-NHCHR_1R_2$, $-OCHR_1R_2$, $-SCHR_1R_2$, $-CHR_1R_2$ or $-NR_1R_2$, R_1 and R_2 of B may form a saturated 5- to 8-membered ring which may optionally contain one

or

two double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen, $S(O)_m$, nitrogen or NR_{12} ; and which carbocyclic ring can optionally be substituted with from 1 to 3 substituents selected from the group consisting of hydroxy, C_1 - C_4 alkyl, fluoro, chloro, bromo, iodo, CF_3 , $-O-(C_1-C_4 \text{ alkyl})$, $-O-CO-(C_1-C_4 \text{ alkyl})$, $-O-CO-NH(C_1-C_4 \text{ alkyl})$, $-O-CO-N(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-NH(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_4 \text{ alkyl})$, $-S(C_1-C_4 \text{ alkyl})$, $-N(C_1-C_4 \text{ alkyl})CO(C_1-C_4 \text{ alkyl})$, $-NHCO(C_1-C_4 \text{ alkyl})$, $-COO(C_1-C_4 \text{ alkyl})$, $-CONH(C_1-C_4 \text{ alkyl})$, $-CON(C_1-C_4 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, CN , NO_2 , $-OSO_2(C_1-C_4 \text{ alkyl})$, $-SO(C_1-C_4 \text{ alkyl})$, and $-SO(C_1-C_4 \text{ alkyl})$, wherein one of said one to three substituents can further be selected from phenyl;

R_3 is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF_3 , NH_2 , $NH(C_1-C_2 \text{ alkyl})$, $N(CH_3)_2$, $-NHCOCF_3$, $-NHCH_2CF_3$, $S(O)_m(C_1-C_4 \text{ alkyl})$, $CONH_2$, $-CONHCH_3$, $CON(CH_3)_2$, $-CF_3$, or CH_2OCH_3 ;

R_4 is hydrogen, C_1 - C_4 hydrocarbyl, C_3 - C_5 cycloalkyl, $-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_5 \text{ cycloalkyl})$, $-(C_3-C_5 \text{ cycloalkylene})(C_3-C_6 \text{ cycloalkyl})$, cyano, fluoro, chloro, bromo, iodo, $-OR_{24}$, C_1 - C_6 alkoxy, $-O-$ cycloalkyl, $-O-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_5 \text{ cycloalkyl})$, $-O-(C_3-C_5 \text{ cycloalkylene})(C_3-C_5 \text{ cycloalkyl})$, $-CH_2SC(S)O(C_1-C_4 \text{ alkyl})$, CH_2OCF_3 , CF_3 , amino, nitro, $-NR_{24}R_{25}$, $-(C_1-C_4 \text{ hydrocarbylene})-OR_{24}$, $-(C_1-C_4 \text{ hydrocarbylene})Cl$, $-(C_1-C_4 \text{ hydrocarbylene})NR_{24}R_{25}$, $-NHCOR_{24}$, $-NHCONR_{24}R_{25}$, $-CH=NOR_{24}$, $-NHN R_{24}R_{25}$, $-S(O)_mR_{24}$, $-C(O)R_{24}$, $-OC(O)R_{24}$, $-C(O)CN$, $-C(O)NR_{24}R_{25}$, $-C(O)NHN R_{24}R_{25}$, and $-COOR_{24}$, wherein the hydrocarbyl and hydrocarbylene groups of R_4 may optionally independently contain one or two double or triple bonds and may optionally independently be substituted with one or two substituents R_{10} independently selected from hydroxy, amino, $-NHCOCCH_3$, $-NHCOCCH_2Cl$, $-NH(C_1-C_2 \text{ alkyl})$, $-N(C_1-C_2 \text{ alkyl})(C_1-C_2 \text{ alkyl})$, $-COO(C_1-C_4 \text{ alkyl})$, $-COOH$, $-CO(C_1-C_4 \text{ alkyl})$, C_1 - C_6 alkoxy, C_1 - C_3 thioalkyl, cyano and nitro, and with one to four substituents independently selected from fluoro and chloro;

R_5 is aryl or heteroaryl and is substituted with from one to four substituents R_{27} independently selected from halo, C_1 - C_{10} hydrocarbyl, $-(C_1-C_4 \text{ hydrocarbylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_1-C_4 \text{ hydrocarbylene})(C_4-C_8 \text{ heterocycloalkyl})$, $-(C_3-C_8 \text{ cycloalkyl})$, $-(C_4-C_8 \text{ heterocycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_3-C_8 \text{ cycloalkyl})$, $-(C_3-C_8 \text{ cycloalkylene})(C_4-C_8 \text{ heterocycloalkyl})$, C_1 - C_4 haloalkyl, C_1 - C_4 haloalkoxy, nitro, cyano, $-NR_{24}R_{25}$, $-NR_{24}COR_{25}$, $-NR_{24}CO_2R_{26}$, $-COR_{24}$, $-OR_{25}$, $-CONR_{24}R_{25}$, $-CON(OR_{22})R_{23}$, $-CO_2R_{26}$, $-C=N(OR_{22})R_{23}$, and $-S(O)_mR_{23}$; wherein said C_1 - C_{10} alkyl, C_3 - C_8 cycloalkyl, $(C_1-C_4 \text{ hydrocarbylene})$, $(C_3-C_8 \text{ cycloalkyl})$, $(C_3-C_8 \text{ cycloalkylene})$, and $(C_4-C_8 \text{ heterocycloalkyl})$ groups can be optionally substituted with from one to three substituents independently selected from C_1 - C_4 alkyl, C_3 - C_8

cycloalkyl, (C₁-C₄ hydrocarbylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), C₁-C₄ haloalkyl, hydroxy, C₁-C₆ alkoxy, nitro, halo, cyano, -NR₂₄R₂₅, -NR₂₄COR₂₅, NR₂₄CO₂R₂₆, -COR₂₄, -OR₂₅, -CONR₂₄R₂₅, CO₂R₂₆, -CO(NOR₂₂)R₂₅, and -S(O)_mR₂₃; and wherein two adjacent substituents of the R₅ group can optionally form a 5-7 membered ring, saturated or unsaturated, fused to R₅, which ring optionally can contain one, two, or three heterologous members independently selected from O, S(O)_m, and N, but not any -S-S-, -O-O-, -S-O-, or -N-S- bonds, and which ring is optionally substituted with C₁-C₄ alkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), C₁-C₄ haloalkyl, nitro, halo, cyano -NR₂₄R₂₅, NR₂₄COR₂₅, NR₂₄CO₂R₂₆, -COR₂₄, -OR₂₅, -CONR₂₄R₂₅, CO₂R₂₆, -CO(NOR₂₆)R₂₅, or -S(O)_mR₂₃; wherein one of said one to four optional substituents R₂₇, can further be selected from -SO₂NH(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), SO₂NH(C₃-C₈ cycloalkyl), -SO₂NH(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -NHSO₂(C₃-C₈ cycloalkyl), -NHSO₂(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), and -NHSO₂(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl); and wherein the hydrocarbyl, and hydrocarbylene groups of R₅ may independently optionally contain one double or triple bond;

R₆ is hydrogen, C₁-C₆ alkyl, C₃-C₈ cycloalkyl, -(C₁-C₆ alkylene)(C₃-C₈ cycloalkyl), or -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), wherein said alkyl and cycloalkyl may optionally be substituted with one hydroxy, methoxy, ethoxy or fluoro group;

or R₆ and R₄ can together form an oxo (=O) group, or can be connected to form a 3-8 membered carbocyclic ring, optionally containing one to three double bonds, and optionally containing one, two, or three heterologous ring members selected from O, SO_m, N, and NR₁₂, but not containing any -O-O-, -S-O-, -S-S-, or -N-S- bonds, and further optionally substituted with C₁-C₄ hydrocarbyl or C₃-C₆ cycloalkyl, wherein said C₁-C₄ hydrocarbyl substituent may optionally contain one double or triple bond;

R₁₁ is hydrogen, hydroxy, fluoro, ethoxy, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl;

R₂₂ is independently at each occurrence selected from hydrogen, C₁-C₁₄ alkyl, C₁-C₁₄ haloalkyl, C₃-C₆ alkenyl, C₃-C₆ alkynyl, C₃-C₈ cycloalkyl, (C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), and (C₁-C₄ alkylene)(C₃-C₈ cycloalkyl);

R₂₃ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₂-C₈ alkoxyalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, -(C₁-C₄ alkylene)aryl, piperidine, pyrrolidine, piperazine, N-methylpiperazine, morpholine, and thiomorpholine;

R₂₄ and R₂₅ are independently at each occurrence selected from hydrogen, -C₁-C₄ alkyl,

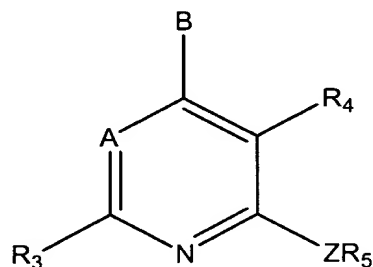
C₁-C₄ haloalkyl, -(C₁-C₄ alkylene)OH, -(C₁-C₄ alkylene)-O-(C₁-C₄ alkyl), -(C₁-C₄ alkylene)-O-(C₃-C₅ cycloalkyl), C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), -C₄-C₈ heterocyclohydrocarbyl, -(C₁-C₄ alkylene)(C₄-C₈ heterocyclohydrocarbyl), -(C₃-C₈ cycloalkylene)(C₄-C₈ heterocyclohydrocarbyl), aryl, and -(C₁-C₄ alkylene)(aryl), wherein the -C₄-C₈ heterocyclohydrocarbyl groups can each independently optionally be substituted with aryl, CH₂-aryl, or C₁-C₄ alkyl, and can optionally contain one or two double or triple bonds; or, when R₂₄ and R₂₅ are as NR₂₄R₂₅, -C(O)NR₂₄R₂₅, -(C₁-C₄ alkylene)NR₂₄R₂₅, or -NHCONR₂₄R₂₅, then NR₂₄R₂₅ may further optionally form a 4 to 8 membered heterocyclic ring optionally containing one or two further hetero members independently selected from S(O)_m, oxygen, nitrogen, and NR₁₂, and optionally containing from one to three double bonds;

R₂₆ is independently at each occurrence selected from C₁-C₄ alkyl, C₁-C₄ haloalkyl, C₃-C₈ cycloalkyl, -(C₁-C₄ alkylene)(C₃-C₈ cycloalkyl), -(C₃-C₈ cycloalkylene)(C₃-C₈ cycloalkyl), aryl, and -(C₁-C₄ alkylene)(aryl); and

wherein each m is independently zero, one, or two,

with the proviso that heterocyclohydrocarbylene groups of the compound of formula I, do not comprise any -S-S-, -S-O-, -N-S-, or -O-O- bonds, and do not comprise more than two oxygen or S(O)_m heterologous members.

Claim 2 (Twice Amended). A compound according to claim 1 of the formula



or a pharmaceutically acceptable salt thereof, wherein

A is N;

B is -NR₁R₂, -CR₁R₂R₁₁, -C(=CR₂R₁₂)R₁, -NHCHR₁R₂, -OCHR₁R₂, -SCHR₁R₂, -CHR₂OR₁₂, -CHR₂SR₁₂, -C(S)R₂ or -C(O)R₂;

Z is -NH, O, S, N(C₁-C₂ alkyl) or C(R₁₃R₁₄) wherein R₁₃ and R₁₄ are each independently, hydrogen, trifluoromethyl or methyl or one of R₁₃ and R₁₄ is cyano and the other is hydrogen or methyl;

R₁ is C₁-C₆ hydrocarbyl which may optionally be substituted with one or two substituents

R₈ independently selected from the group consisting of hydroxy, fluoro, chloro, bromo, iodo, CF₃, C₁-C₄ alkoxy, -O-CO-(C₁-C₄ hydrocarbyl), -O-CO-NH(C₁-C₄ hydrocarbyl), -O-CO-N(C₁-C₄ hydrocarbyl)(C₁-C₂ hydrocarbyl), -NH(C₁-C₄ hydrocarbyl), -N(C₁-C₂ alkyl)(C₁-C₄ hydrocarbyl), -S(C₁-C₄ alkyl), -N(C₁-C₄)CO(C₁-C₄ hydrocarbyl), -NHCO(C₁-C₄ hydrocarbyl), -COO(C₁-C₄ hydrocarbyl)hydrocarbyl, -CONH(C₁-C₄ hydrocarbyl), -CON(C₁-C₄ hydrocarbyl)(C₁-C₂ alkyl), CN, NO₂, -SO(C₁-C₄ hydrocarbyl) and -SO₂(C₁-C₄ hydrocarbyl), and wherein said C₁-C₆ hydrocarbyl and the (C₁-C₄)hydrocarbyl moieties in the foregoing R₁ groups may optionally contain one carbon-carbon double or triple bond;

R₂ is C₁-C₁₂ hydrocarbyl, aryl or -(C₁-C₄ hydrocarbylene)aryl wherein said aryl is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl, imidazolyl, furanyl, benzofuranyl, benzothiazolyl, isothiazolyl, benzisothiazolyl, benzisoxazolyl, benzimidazolyl, indolyl, or benzoxazolyl; 3- to 8-membered cycloalkyl or -(C₁-C₆ alkylene)cycloalkyl, wherein one or two of the ring carbons of said cycloalkyl having at least 4 ring members and the cycloalkyl moiety of said -(C₁-C₆ alkylene)cycloalkyl having at least 4 ring members may optionally be replaced by an oxygen or sulfur atom or by N-R₉ wherein R₉ is hydrogen or C₁-C₄ alkyl; and wherein each of the foregoing R₂ groups may optionally be substituted with from one to three substituents independently selected from chloro, fluoro and C₁-C₄ alkyl, or with one substituent selected from bromo, iodo, C₁-C₆ alkoxy, -O-CO-(C₁-C₆ alkyl), -O-CO-N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -S(C₁-C₆ alkyl), CN, NO₂, -SO(C₁-C₄ alkyl), and -SO₂(C₁-C₄ alkyl), and wherein said C₁-C₁₂ hydrocarbyl and the C₁-C₄ hydrocarbylene moiety of said -(C₁-C₄ hydrocarbylene)aryl may optionally contain one carbon-carbon double or triple bond;

or -NR₁R₂ or -CR₁R₂R₁₁ may form a saturated 5- to 8-membered carbocyclic ring which may optionally contain one or two carbon-carbon double bonds and in which one or two of the ring carbons may optionally be replaced by an oxygen or sulfur atom;

R₃ is methyl, ethyl, fluoro, chloro, bromo, iodo, cyano, methoxy, OCF₃, methylthio, methylsulfonyl, CH₂OH, or CH₂OCH₃;

R₄ is hydrogen, C₁-C₄ hydrocarbyl, fluoro, chloro, bromo, iodo, C₁-C₄ alkoxy, trifluoromethoxy, -CH₂OCH₃, -CH₂OCH₂CH₃, -CH₂CH₂OCH₃, -CH₂OF₃, CF₃, amino, nitro, -NH(C₁-C₄ alkyl), -N(CH₃)₂, -NHCOCH₃, -NHCONHCH₃, -SO_n(C₁-C₄ hydrocarbyl) wherein n is 0, 1 or 2, cyano, hydroxy, -CO(C₁-C₄ hydrocarbyl), -CHO, cyano or -COO(C₁-C₄ alkyl) wherein said C₁-C₄ hydrocarbyl may optionally contain one double or triple bond and may optionally be substituted with one substituent selected from hydroxy, amino, -NHCOCH₃, -NH(C₁-C₂ alkyl), -N(C₁-C₂ alkyl)₂, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), C₁-C₃ alkoxy, C₁-C₃ thioalkyl, fluoro, chloro, cyano and nitro;

R₅ is phenyl, naphthyl, thienyl, benzothienyl, pyridyl, quinolyl, pyrazinyl, pyrimidyl,

furanyl, benzofuranyl, benzothiazolyl, or indolyl, wherein each of the above groups R₅ is substituted with from one to three substituents independently selected from fluoro, chloro, C₁-C₆ alkyl, and C₁-C₆ alkoxy, or with one substituent selected from hydroxy, iodo, bromo, formyl, cyano, nitro, trifluoromethyl, amino, -(C₁-C₆ alkyl)O(C₁-C₆)alkyl, -NHCH₃, -N(CH₃)₂, -COOH, -COO(C₁-C₄ alkyl), -CO(C₁-C₄ alkyl), -SO₂NH(C₁-C₄ alkyl), -SO₂N(C₁-C₄ alkyl)(C₁-C₂ alkyl), -SO₂NH₂, -NHSO₂(C₁-C₄ alkyl), -S(C₁-C₆ alkyl) and [-SO₂(C₁-C₆ alkyl)] -SO₂(C₁-C₆ alkyl), and wherein the C₁-C₄ alkyl and C₁-C₆ alkyl moieties of the foregoing R₅ groups may optionally be substituted with one or two fluoro groups or with one substituent selected from hydroxy, amino, methylamino, dimethylamino and acetyl;

R₁₁ is hydrogen, hydroxy, fluoro, or methoxy;

R₁₂ is hydrogen or C₁-C₄ alkyl; and

or a pharmaceutically acceptable salt of such compound.

Claim 12 (Amended). A compound according to claim 1, wherein said compound is selected from the group consisting of:

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-diethyl-amine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-propyl-amine;

butyl-[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-amine;

4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethyl-phenylsulfanyl)-pyridine;

butyl-[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-ethyl-amine;

[3,6-dimethyl-[2-(2,4,6-trimethyl-phenylsulfanyl)-pyridin-4-yl]-ethyl-propyl-amine;

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-ethyl-propyl-amine;

N4-(1-ethyl-propyl)-6-methyl-3-nitro-N2-(2,4,6-trimethyl-phenyl)-pyridine-2,4-diamine;

3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-ethyl-(2,2,2-trifluoro-ethyl)-amine;

N4-(1-ethyl-propyl)-6-methyl-N2-(2,4,6-trimethyl-phenyl)-pyridine-2,3,4-triamine;

(N-(1-ethyl-propyl)-2-methyl-5-nitro-N'-(2,4,6-trimethyl-pyridin-3-yl)-pyrimidine-4,6-diamine;

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-diethyl-amine;

(1-ethyl-propyl)-[5-methyl-3-(2,4,6-trimethyl-phenyl)-3H-imidazo [4,5-b]pyridin-7-yl-amine;

[2,5-dimethyl-3-(2,4,6-trimethyl-phenyl)-3H-imidazo[4,5-b]pyridin-4-yl]-(1-ethyl-propyl)-amine; [or]

[4-(1-ethyl-propoxy)-3,6-dimethyl-pyridin-2-yl]-(2,4,6-trimethylphenyl)-amine;

[4-(1-ethyl-propoxy)-3,6-dimethyl-2-(2,4,6-trimethylphenoxy)-pyridine;

[3,6-dimethyl-2-(2,4,6-trimethyl-phenoxy)-pyridin-4-yl]-(1-ethyl-propyl)-amine; and

[2-(4-chloro-2,6-dimethyl-phenoxy)-3,6-dimethyl-pyridin-4-yl]-(1-ethyl-propyl)-amine

or pharmaceutically acceptable salt of one of the above compounds.

Claim 13 (Twice Amended). A pharmaceutical composition for the treatment of (a) a disorder or condition the treatment of which can be effected or facilitated by antagonizing CRF or (b) a disorder or condition selected from inflammatory disorders, pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive-compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception [such as fibromyalgia]; mood disorders, mood disorders associated with premenstrual syndrome, and postpartum depression; dysthemia; bipolar disorders; cyclothymia; chronic fatigue syndrome; stress-induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; post operative ileus; ulcer; diarrhea; stress-induced fever; human immunodeficiency virus infections; neurodegenerative diseases, gastrointestinal diseases; eating disorder; hemorrhagic stress; chemical dependencies or addictions; drug or alcohol withdrawal symptoms; stress-induced psychotic episodes; euthyroid sick syndrome; syndrome of inappropriate antidiuretic hormone; obesity; infertility; head trauma; spinal cord trauma; ischemic neuronal damage, [including cerebral ischemia;] epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; hypertension; tachycardia; congestive heart failure; osteoporosis; premature birth; hypoglycemia, and Syndrome X in a mammal or bird, comprising an amount of a compound according to claim 1 that is effective in the treatment of such disorder or condition, and a pharmaceutically acceptable carrier.

Claim 14 (Twice Amended). A pharmaceutical composition according to claim 13 for the treatment of a disorder selected from inflammatory disorders; pain, asthma, psoriasis and allergies; generalized anxiety disorder; panic; phobias; obsessive compulsive disorder; post-traumatic stress disorder; sleep disorders induced by stress; pain perception; mood disorders [such as depression,, and postpartum depression]; dysthemia; bipolar disorders; cyclothymia; fatigue syndrome; stress induced headache; cancer; irritable bowel syndrome, Crohn's disease; spastic colon; human immunodeficiency virus (HIV) infections; neurodegenerative diseases; gastrointestinal diseases; eating disorders; chemical dependencies and addictions; obesity; infertility; head traumas; spinal cord trauma; ischemic neuronal damage; excitotoxic neuronal damage; epilepsy; stroke; immune dysfunctions; muscular spasms; urinary incontinence; senile dementia of the Alzheimer's type; multi infarct dementia; amyotrophic lateral sclerosis; and hypoglycemia in a mammal[, including a human].

Claim 29 (Amended). A compound as claimed in claim 1 wherein [R24 and R25]
R₂₄ and R₂₅ are selected from -CF₃, -CHF₂, CF₂CF₃, and CH₂CF₃,

Claim 32 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of depression, selected from the group consisting of major depression, single episode depression, recurrent depression, and child abuse induced depression.

Claim 36 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of [stress induced] immune dysfunctions induced by stress selected from the group consisting of [including] porcine stress syndrome, bovine shipping fever, equine paroxysmal fibrillation, confinement dysfunction in chicken, sheering stress in sheep, and human animal interaction stress in dogs.

Claim 40 (Amended). A pharmaceutical composition as claimed in claim 14 for treatment of social phobia, agoraphobia, or specific phobias.